REMARKS

Applicants have received and reviewed an Office Action dated February 20, 2004. Acceptance of the Request for Continued Examination and withdrawal of finality of the previous Office Action is acknowledged. Applicants thank the Examiner for his consideration of the Information Disclosure Statement filed on May 6, 2003. Applicants request entry of this Response and reconsideration of the rejection of the claims.

Claims 2-4, 8-11, 15-21, and 96-101 are currently pending.

Claims 1, 5-7, 12-14, 17, and 22-95 are canceled without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of these claims in one or more continuation applications. Applicants' indication on page 6 of the 11/21/03 Response that claims 7-11 were canceled was a typographical error inconsistent with the listing of the claims in that Response.

Claims 2, 3, 4, 8, 9, 15, 96 and 99 are amended. Support for the amendments can be found throughout the specification including at page 8, lines 4-5, page 121, lines 4-7, Fig. 2 and Fig..9. Applicants submit the amendments to the claims do not raise any issues of new matter. With respect to all amendments, Applicants have not dedicated or abandoned any unclaimed subject matter and have not acquiesced to any objection and/or rejection made by the Examiner. Applicants expressly reserve the right to pursue the canceled subject matter in one or more continuation applications.

Claims 102 to 106 are added. Support for the new claims can be found throughout the specification including at pages 100-104, pages 132-135. Applicants submit the new claims do not raise any issues of new matter.

The Examiner indicated in the Office Action Summary that all pending claims: 1-4, 7-11, 15, 16, 18-21 and 96-101 are rejected. However, reasons for rejection were presented only for claims 1,7, 9-11, 15, 16, 18-21 and 96-101. In light of the Examiner's statements regarding the claims that are addressed, Applicant's will assume that claims 2-4, and 8 are rejected only the basis of being dependent on rejected independent claims.

Claims 2-4 and 8 are now presented in independent form. The Examiner did not present reasons for rejection of claims 2-4, and 8 in the Office Action of 2/20/04 and has made

statements indicating that SEQ ID NO:1 is sufficiently described, enabled and not anticipated. In light of those statements, Applicants respectfully request allowance of claims 2-4 and 8 in present form.

Petition for Extension of Time

It is noted that a 2-month petition for extension of time is necessary to provide for timeliness of the response. A request for such an extension is made extending the time for response from May 20, 2004 to July 20, 2004.

Information Disclosure Statement

Applicants advise the Examiner that a Supplemental Information Disclosure Statement will be submitted within the next two weeks.

Claim for Domestic Priority

Applicants request that the Examiner acknowledge Applicants' claim for domestic priority under 35 U.S.C. § 119(e) to 60/228,914 filed August 29, 2000, 60/197,089 filed April 14, 2000, and 60/175,849 filed January 13, 2000.

35 U.S.C. § 112, First paragraph, Written Description

Claims 1, 7,15, 16, 18-21 and 96-101 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner contends, while the specification meets written description for the nucleotide sequence of SEQ ID NO:1 (which encodes SEQ ID NO:2), it does not provide written description for polynucleotides having at least 80% sequence identity to disclosed sequences. The Examiner cites Skolnick et al for the proposition that assigning a functional activity based on sequence homology is inaccurate and further alleges that any sequence similarity other than 100% results in an unpredictable and, therefore, unreliable correspondence between the newly discovered sequence and a similar biomolecule of known function or expression. In addition, the Examiner asserts that describing a

method of preparing a cDNA or even describing the protein that the cDNA encodes, which the Examiner acknowledges the example does, does not necessarily describe the cDNA itself. Applicants have canceled claims 1 and 7 without prejudice or disclaimer, rendering the rejection of these claims moot. Applicants respectfully traverse the rejection with respect to the other claims.

The written description requirement is satisfied when Applicants' specification conveys with reasonable clarity to those skilled in the art, that as of the filing date sought, he or she was in possession of the invention. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). A written description of an invention involving a chemical genus requires a precise definition, such as by structure, formula ... of the claimed subject matter sufficient to distinguish it from other materials. Univ. of California v. Eli Lilly and Co., 43 USPQ2d 1398. 1405 (Fed. Cir. 1997) (emphasis added). Since one skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass, such a formula is normally an adequate description of the claimed invention. Id. at 1406 (emphasis added).

Moreover, as noted in the Guidelines for Examination of Patent Applications Under 35 U.S.C. § 112, ¶1, "Written Description" Requirement ("the guidelines"), there is a "strong presumption" that an adequate written description of the claimed invention is present when the application is filed, 66(4) Fed Reg. 1099, 1105 (2001); see also, In re Wertheim, 191 USPQ 90,97 (CCPA 1976). The guidelines further state that "[(The examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims." 66(4) Fed. Reg. at 1107; 191 USPQ at 97, (emphasis added).

Claim 96 relates to a genus of nucleic acid molecules which comprise DNA having at least 99% sequence identity to (a) a DNA molecule encoding a PRO10282 polypeptide comprising the sequence of amino acid residues from 1 to 667 of Figure 2 (SEQ ID NO:2), or (b) the complement of the DNA molecule of (a), wherein the isolated nucleic acid molecule encodes a polypeptide having 9 potential transmembrane domains as indicated by the hydrophobicity plot for PRO10282 polypeptide comprising the sequence of amino acid residues 1 to 667 of Figure 2 (SEQ ID NO:2) in FIG.9. Claim 99 relates to a genus of nucleic acid molecules comprising DNA which comprises at least 99% sequence identity to (a) the full-length polypeptide coding

sequence of the human protein cDNA deposited with the ATCC on January 11,2000 under ATCC Deposit No. PTA-1181 (DNA148380-2827), or (b) the complement of the coding sequence of (a), wherein the isolated nucleic acid molecule encodes a polypeptide having 9 potential transmembrane domains as indicated by the hydrophobicity plot for PRO10282 polypeptide comprising the sequence of amino acid residues 1 to 667 of Figure 2 (SEQ ID NO:2) in FIG.9.

As an initial matter, in contrast to the Examiner's position, Applicants have described the structure of a nucleic acid and have not just provided a method for obtaining the cDNA. Applicants have disclosed and described a nucleic acid molecule comprising SEQ ID NO:1. Applicants have also deposited human protein cDNA ATCC Deposit No. PTA-1181 (DNA148380-2827). It is within the purview of one of skill in the art to determine the sequence of the deposited material. As discussed previously, once in possession of this sequence, a person of skill in the art could in the least readily envision all the DNAs degenerate to SEQ ID NO:1 or that of the deposited material, and therefore would conclude that the applicant was in possession of the genus of DNAs that have at least 99% sequence identity to a DNA molecule encoding a PRO10282 polypeptide comprising SEQ ID NO:2 or the amino acid sequence of the deposited material. DNAs related by a specific percentage identity are readily ascertained by one of skill in the art by making a direct comparison of the sequences. One of skill in the art can readily envision the genus of nucleic acid molecules comprising DNA having at least 99% sequence identity to the ATCC Deposited material by applying nucleic acid base pair matching, a genetic code table, and sequence alignment and identity tools. Tools for quickly measuring sequence alignment and identity are commonly used by those of skill in the art, for example BLAST, BLAST-2, ALIGN, ALIGN-2 and Megalign (DNASTAR). Consequently, one of skill in the art would not only ascertain that the applicant was in possession of the genus of DNAs encoding the protein of SEQ ID NO:2 and their complements, but also in possession of DNAs having at least 99% identity to that genus. Therefore, Applicants submit claims 96 and 99 meet the written description requirement.

The Examiner contends that it is unpredictable to identify sequences with similarity of less than 100%. Applicants disagree. Applicants submit that a naturally occurring variant, shown in Figures 6 and 7 (SEQ ID NO:4), has about 99% nucleotide sequence identity to SEQ ID

NO:1 is described in the application and was readily identified. In addition, Applicants have directed one of skill in the art to align the sequence of SEQ ID NO:2 with that of homologous protein molecules and minimize the number of amino acid sequence regions of high identity. (See the specification at page 46, line 28 to page 47, line 6). In Figure 8, Applicants have provided alignment of SEQ ID NO:2 with murine stra6 sequence and the variant sequence. Such alignment can be readily conducted with the murine stra6 sequence and variant stra6 sequence as provided by Applicants.

In addition, Applicants dispute the contention that the Skolnick et al reference establishes that in all cases assigning function based on sequence homology is inaccurate. Applicants submit that the Skolnick et al reference is a general reference and does not specifically refer to stra6 polypeptides. There is no teaching or suggestion that this reference can be applied to every protein family. Secondly, Applicants have provided more than sequence information in this application. Applicants have provided information about the structure as well as an information that would alow one of skill in the skill to prepare an alignment to other related sequences. In addition, the Skolnick et al. reference does not say that no functionality can be assigned but only that multiple functions may be difficult to assign. Finally, Applicants submit that others have shown the identification of homologs based on at least 30% sequence identity. (See Brenner et al, copy attached).

Furthermore, claims 96 and 99 are amended to provide that the encoded polypeptide to has similar structural features of that of PRO10282 polypeptide. Specifically, the claim recites that the encoded polypeptide has 9 potential transmembrane domains as indicated by the hydrophobicity plot of figure 9.

Claims 97 and 98 are dependent on claim 96 and are rejected by the Examiner on the same grounds as claim 96. Claims 97 and 98 are directed to particular sequences that have the claimed "at least 99% identity" of claim 96. As claims 97 and 98 are directed to particular sequences, which are fully supported in the specification, claims 97 and 98 meet the § 112 written description requirement.

Claims 15 and 16 do not include % identity language except to the extent to which they rely on other claims. Claims 15 and 16 are amended to refer to claims 2-4 and 8-11, which do not include % identity language. Because claims 2-4 and 8-11 are not rejected under §112¶1, and

the other subject matter of claims 15 and 16 is supported in the specification, the Examiner is respectfully requested to withdraw his rejection.

The Examiner contends that the claims are not drawn to a genus of polynucleotides encoding a particular protein, but Applicants submit that the written description does not require that the isolated nucleic acid molecule encode a particular protein, but only that description allow one of skill in the art to distinguish it from other materials. Applicants submit they have described the isolated nucleic acid sequences sufficiently to allow one of skill in the art to distinguish the claimed subject matter. As discussed above, Applicants have described and provided a structural formula for a species, which has been fully reduced to practice.

Based on the foregoing, Applicants respectfully request withdrawal of this rejection.

35 U.S.C. § 112, First paragraph, Enablement

Claims 1, 7, 15, 16, 18-21 and 96-101 were rejected under 35 U.S.C. § 112, first paragraph, because the Examiner contends that the specification, while being enabling for the nucleotide sequence of SEQ ID NO:1, does not reasonably provide enablement for polynucleotides having at least certain % identity because there is not sufficient guidance as to how to use the polynucleotides. Applicants have canceled claims 1 and 7 without prejudice or disclaimer. Applicants respectfully traverse with respect to the other claims.

The legal standard for enablement under 35 U.S.C. § 112 requires that "[...] a patent specification must disclose sufficient information to enable **those skilled in the art** to make the claimed invention." *Hormone Research Foundation, Inc. v. Genentech*, 15 USPQ2d 1039, 1047 (Fed. Cir. 1990). It is a well accepted premise that §112¶1 requires only that a patent specification describe to one of ordinary skill in the art how to make and use the claimed invention without **undue** experimentation.

The Examiner acknowledges that the specification is enabling for the nucleotide sequence of SEQ ID NO:1 (which encodes protein SEQ ID NO:2). In addition to the nucleotide sequence of SEQ ID NO:1, claim 96 also encompasses polynucleotides having at least 99% sequence identity to sequences encoding a polypeptide of SEQ ID NO:2. Claim 99 also encompasses polynucleotides having at least 99% sequence identity to sequences encoding for the polypeptide encoded by cDNA of ATCC deposit PTA-1181. The Examiner's contention

that lack of expression information for polynucleotides other than SEQ ID NO:1 encompassed by the claims invention does not support an enablement rejection.

Applicants agree with the Examiner that the specification teaches that the polynucleotide of SEQ ID NO:1 is over-expressed in cancer tissues and thus can be used in cancer diagnostics. However, applicants disagree with the Examiner basing his rejection at least in part on the alleged lack of information about over expression of other polynucleotides. Under the law of enablement, a specification that teaches how to make and use the invention in terms, which correspond, in scope to the claims must be taken as satisfying the enablement requirement unless there is reason to doubt the objective truth of the specification. In re Marzocchi, 169 USPQ 367, 369 (CCPA 1971). It is incumbent upon the Examiner to explain why one skilled in the art would doubt the truth of statements made in the specification, and provide back up assertions with acceptable evidence or reasoning which is inconsistent with the teachings of the specification. Id.at 370. Absent evidence to the contrary, the specification must be assumed to be enabling.

Independent claims 96 and 99 are further supported by a naturally occurring variant, PRO19578 shown in Figures 6 and 7 (SEQ ID NO:4) that has about 99% nucleotide sequence identity to SEQ ID NO:1. The alignment between amino acid sequence (SEQ ID NO:2), the variant (SEQ ID NO:4), and the murine stra6 sequence identifies regions of high identity of the molecule. The use of the variant sequence is also supported in the specification to allow one of skill in the art to make and use it. For example, Example 2 at page 121 provides a method of using PRO19578 as a hybridization probe. For the description of the variant sequence, one of skill in the art can make use of this and other variants in the same manner as SEQ ID NO:1. It would be routine for one skilled in the art to identify nucleic acid molecules capable of use for detecting a target polynucleotide.

Thus, Applicants submit that they have provided sufficient description to allow one of skill in the art to make and use the claimed nucleic acids, and respectfully request withdrawal of the 35 U.S.C. § 112, first paragraph, rejection.

35 U.S.C. § 112, First Paragraph, New Matter

The rejection of claims 1 and 7 under 35 U.S.C. § 112, first paragraph, is moot as those claims have been canceled, rendering the rejection of these claims moot.

Claims 9-11 were rejected under 35 U.S.C. § 112, first paragraph for the introduction of new matter. Specifically, the Examiner indicates the amendment to claim 9 adding the limitation of the PRO10282 polypeptide encoded by the claimed nucleic acid is at least 100 amino acids introduced new matter. Claims 10 and 11 are dependent on claim 9. The Examiner further indicated that the specification does not specifically teach that nucleic acids that hybridize to complement DNA encoding protein SEQ ID NO:2 must encode a fragment of not less than 100 residues. Applicants respectfully traverse.

The standard for support of added claim limitations under 35 USC § 112¶1 indicates that disclosure to support an amendment to a claim, may be express, implicit or inherent. MPEP §2163 (IB). Information contained in the specification, claims or drawings of an application as filed may be added to any other part of the application without introducing new matter. MPEP §2163.06. Support sufficient enough to meet 35 U.S.C. § 112, first paragraph, need not be *ipsis verbis* [i.e., "in the same words"] to be sufficient.

The specification, at page 33 line 24-29, describes that variant polynucleotides are nucleic acid molecules that encode an active PRO10282 polypeptide and which are capable of hybridizing, preferably under stringent conditions to nucleotide sequences encoding full-length PRO10282 polypeptides shown in Figure 2 (SEQ ID NO:2). PRO10282 variant polypeptides may be those that are encoded by a PRO10282 variant polynucleotide. In the present application, support for the PRO10282 polypeptide to be at least 100 amino acids in length is found on page 27, which describes a variety of lengths available for PRO10282 variants. Moreover, the specification describes that another embodiment is directed to fragments of a PRO 10282 polypeptide coding sequence that may find use as hybridization probes. These fragments can be at least 300 nucleotides in length. It is known to those of skill in the art that a coding sequence of 300 nucleotides in length encodes a polypeptide of 100 amino acids. (See the specification at page 12 lines 15 to page 13, line 10.

The portions of the specification cited above duly support hybridization to a PRO10282 polypeptide being at least 100 amino acids in length, in a sufficient manner for one of skill in the art to recognize the inventors having possession of the claimed invention at the time of filing.

Other amended language in claim 9 is also not new matter. The relevant language in claim 9 is: "wherein the isolated nucleic acid is other than DNA encoding a murine stra6 polypeptide". According to MPEP § 2173.01(i) Negative Limitations: A negative limitation must have a basis in the original disclosure, but lack of a literal basis is not sufficient for a *prima facie* case for lack of support. Disclosure to support added claim limitations may be express, implicit or inherent. MPEP §2163 (IB). Support for the language of claims 9-11 is explicitly found on page 8, lines 4-5.

In view of the basis above, the rejection of claims 9-11 under 35 U.S.C. § 112, first paragraph, is respectfully requested to be withdrawn.

35 U.S.C. § 102

The rejection of claims 1, 7, 9 through 11 under 35 U.S.C. § 102(a) as being anticipated by the sequence of Database GenEmbl, accession number AF062476 is withdrawn in view of the amendments to exclude polynucleotides encoding murine stra6 polypeptide. However, the Examiner notes that the amendment has drawn a new matter rejection and will reinstate this rejection if that amendment is withdrawn. Applicants assert that the amendments made to claims 1, 7 and 9-11 are not new matter and have addressed that rejection above. Consequently, substantive arguments regarding the rejection of claims 1, 7 and 9-11 under 35 U.S.C. § 102(a) will not be made in light of this rejection being withdrawn in view of the amendments.

Similarly, rejection of claims 9-11 under 35 U.S.C. § 102(a) is withdrawn in view of the amendment to the claims requiring that the claimed nucleic acids encode at least 100 residues of polypeptide SEQ. ID No. 2. Applicants assert that the amendment made to claims 9-11 is not new matter according to the supporting arguments presented above and therefore will not make substantive arguments regarding the anticipation of claims 9-11 in view of that rejection being withdrawn in view of the amendments to the claims.

Summary

In view of the above amendments and remarks, Applicants respectfully request a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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